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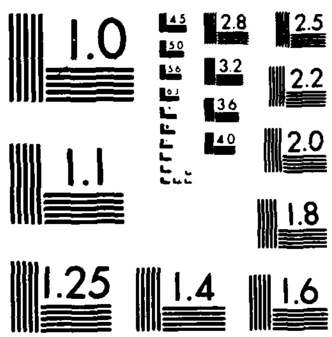
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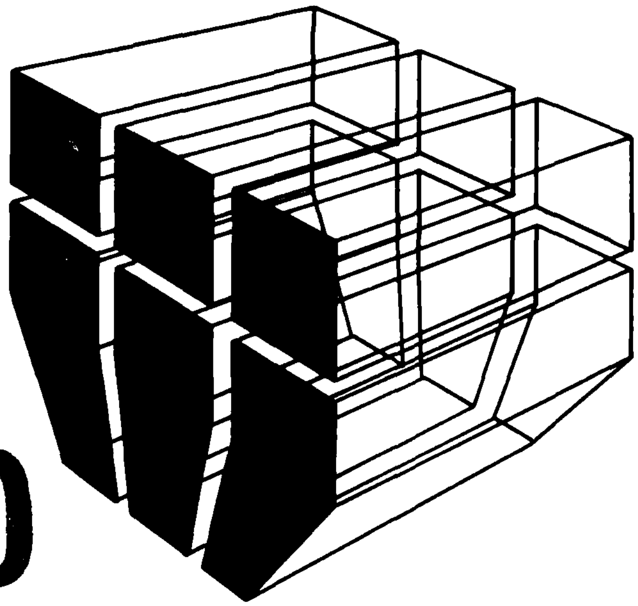

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This paper, "Application of the Guild Concept to Elucidate the Chronic Toxicity of Environmental Pollutants to Man," was presented at the Conference on Applications of the Guild Concept to Environmental Management and should be added to the reader's copy of USA-CERL Technical Manuscript N-86/07, ADA 167190.

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APPLICATION OF THE GUILD CONCEPT TO ELUCIDATE THE CHRONIC TOXICITY OF ENVIRONMENTAL POLLUTANTS TO MAN

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Introduction

Since the industrial revolution, all organisms have been exposed to thousands of new chemical and physical pollutants in their air, water, food, and shelter, and in their work and recreational environments. All life is now chronically exposed to trace quantities of carcinogens, teratogens, and mutagens whose structures have no evolution-based analogs. The impacts of such exposures are insidious, because the exposed populations can neither sense nor prevent them. Also, the insults cannot be decreased through the organisms' detoxification mechanisms. These insults have induced many new diseases, and although such categories of diseases and causes are eventually detected (e. g., Chloracne), it may be too late for much of the population at risk. For example, epidemiological data show that a high percentage of the 5.3 million people who develop some form of cancer each year in the United States do so in response to chemicals. Cancers resulting from tobacco use account for more than 25 percent of the total. Crouch and Wilson (1982, p. 59) estimate that at least 3000 cases of lung cancer per year are caused by polycyclic aromatic hydrocarbons that are found in the air. A large number of cancers and other diseases also occurs in nonhuman species; some types of diseases have devastated certain species.

Although regulatory initiatives have stimulated extensive studies of chemical pollutants' effects on organisms, there has been very little integration and synthesis of the results from nonhuman and human populations. This paper proposes that additional research of new and different scope and experimental design be conducted on chemical pollutants, using the framework of the natural environment as a laboratory. The focus will be the guild, which is defined here as a group of human individuals or a group of nonhuman species that use their environment in a similar way. It is proposed that specific modifications of the guild concept could increase the quality of control population data and thereby increase the likelihood that effects in exposed natural populations can be detected early and attain statistical significance.

Current Methods for Studying Effects in Human Populations

Three major types of studies are routinely used to determine the effects of chemicals on human populations. The most direct evidence is obtained from human epidemiological studies, which include the "informed hunch," follow-up studies, case-control studies, and historical follow-up studies. However, a major problem is that their lack of sensitivity requires either large cohorts or a large effect before detection is possible. Another major problem with epidemiological studies is that the results are based on observations of often irreversible effects already imposed on human populations. To overcome these

problems, the less direct evidence from mammalian studies has been used for centuries to regulate the introduction and use of new chemicals and drugs into the human biosphere. Recently, short-term studies using single-cell and simple nonmammalian species have found a role in testing, prediction, and regulation. Both animal and short-term testing suffer because the artificial environment, high exposure levels, modes of exposure, differences between species, and single-substance testing introduce a presumably large, but unquantifiable, uncertainty with respect to effects on human populations.

Is it possible to overcome any of the disadvantages of the existing studies? What benefits will be derived from overcoming these disadvantages? Are the results from existing studies sufficient to set acceptable policy and regulations in place? It appears that the use of properly described "guilds" to ascertain toxicological effects to human and native species populations from compounds already in the environment affords positive answers.

Applications of the Guild Concept to Controlling Human Exposures

The guild concept has been used, in part, in some of the above-mentioned studies. The historical follow-up study attempts to look at some of the same parameters one would use to classify human populations into "guilds"; for example, occupation, personal habits (such as smoking), and location. However, no comprehensive classification scheme is used consistently, and existing knowledge is too incomplete to suggest one.

Controlled laboratory tests with inbred strains of specific species may be as close as one can come to a simple, and nearly perfect, guild. In fact, in an attempt to eliminate as much variability as possible from laboratory study organisms, genotype, species sensitivity, external and internal environment, route of exposure, and food supply are all kept constant; the only difference is the elimination of the compound being studied from the control group. It is necessary to ensure that the sample size is sufficient to yield statistically sound results, and to keep in mind real-world circumstances, such as primary route of exposure. However, a primary methodology of such studies--the use of exposures far exceeding those occurring in the real environment--makes the test results highly suspect.

To overcome this problem, other experimental designs are needed to supplement and verify laboratory results. An obvious way to ensure that the community at risk is being examined directly is to incorporate the real-world environment into the study design.

If the "guild community" can be analogized to a single organism, one purpose of monitoring will be to establish an organism's "state of health" by identifying existing diseases, disorders, and potentially harmful habits and exposures. After researchers learn how to identify the health of the guild community, they must learn what actions to prescribe to cure the maladies and begin preventive medicine.

To make the environment manageable for this purpose, guilds of natural species must be identified that coexist with man and are exposed in the same way. One example that has received some experimental attention uses wild populations of rodents (mice, rats, voles) inhabiting chemical dumps (Rowley, et al., 1983). An obvious "guild" for this purpose is comprised of small

domestic animals like dogs and cats. For example, R. W. Miller (National Cancer Institute, 1980, PIK) notes that: "The expectation that research into neoplasma among domestic animals would provide new insight into the origins of human cancer led to the establishment of the epizoology section within the clinical epidemiology branch of the National Cancer Institute." Some epidemiological data for these species is available in animal tumor registries (National Cancer Institute, 1980). A better "guild" for examining the effects of environmental contamination is large domestic animals (cows, horses, sheep), because this group is less likely to be affected by other human activities. This group is virtually unnoticed; no epidemiological data were found that compared these species with each other or with man in a coexisting environment.

Some environments may not be useful in elucidating cause-effect relationships because they are uncontrollable. For example, if a major urban environment is viewed in its entirety, no natural "guild" is abundant or representative. Considered together, the individual "guilds" form a community, and it is the community's response that is of epidemiological interest. For example, plants are sensitive monitors of air pollutants, and specific plants can be used to monitor specific pollutants (Anon., 1985). Birds, particularly predators, bioaccumulate many types of chemicals. Tragic experience has shown that exposures within this "guild" often cause species-threatening reductions in number of individuals (for example, eggshell thinning by chlorinated hydrocarbons) (Peakall, 1975). Many insects respond in the opposite way to certain pollutants; i. e., their numbers increase uncontrollably (Coppel and Mertins, 1977). If these "guilds" are considered together as a community, a comprehensive picture of exposure can be developed. The challenge is learning how to interpret these results systematically in terms of ecological community or human epidemiology.

Results from more controllable environments can be useful in applying control measures. Army training lands are currently being used for this purpose. Portions of these lands are routinely exposed to specific chemicals from munitions; however, control communities of natural populations are often available in adjacent areas. The remote or rural locations of these training lands substantially restrict other types of human activity that could compound effects resulting from chemical exposures. Observations of similar communities from control and exposure areas can then be grouped and the study results pooled, compared, and correlated. For example, certain chemical mixtures used in training produce a variety of similar effects (e. g., genetic damage) in laboratory clones of *Tradescantia* spp., natural populations of *Ambrosia dumosa* (Burrobush), and *Dipodomys* spp. (Novak, et al., 1985). The inference is that comparable genetic damage would be observed in exposed humans.

The use of natural "guilds" for epidemiological purposes is implemented through biomonitoring. Biomonitoring is a science with both descriptive and experimental aspects, and it is a set of methods or technologies for gathering data (Herricks, et al., 1986). In applying biomonitoring methods, the investigator must not lose sight of the science required to select the method. The science of biomonitoring requires understanding what a method is measuring, the sensitivity and precision of response at the presumed level of insult, the influence of other environmental factors on the response variable, and the relation of the biomonitor's response to the effect in the human

population of interest. For example, a bacterial assay that tests the mutagenicity of an effluent does not necessarily permit an inference about what its impact on organisms in the receiving stream would be.

Conclusion

The ability to directly monitor the effects of chemicals on human populations is limited. Except where high exposures have produced identifiable illness (e. g., ozone-induced respiratory illness, PCB contamination in Japan), effects on humans are likely to be subtle, cumulative over time, and result from the combined effects of multiple substances. Since the onset of disease is often proportional to the average lifetime of the species, the long human lifetime further complicates the ability to detect diseases induced by environmentally dispersed chemicals. Researchers must learn how to give the "guild community" a complete medical exam, determine the cause of disorders, take action to eliminate the causes, and set up a long-term medical monitoring scheme to ensure health stability. This scheme will drive the type of monitoring that occurs and when it occurs. Research is needed to determine what data thresholds constitute healthy, unhealthy, and average conditions for each guild community. It has been suggested here that valid epidemiological data can be developed by considering "guilds" of species inhabiting the human environment of interest. The challenges are to develop appropriate biomonitoring methods, develop criteria for selecting "guilds," develop monitoring methods for the field that yield consistent, reliable, and understandable data, and develop the understanding necessary to model the human condition from these data. When there are sufficient methods, standards, thresholds, and data from long-term monitoring as well as an understanding of the "guild community's" structural and functional components, researchers will be in a position to prescribe treatment and, from knowledge of causes, prescribe measures to prevent further damage.

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